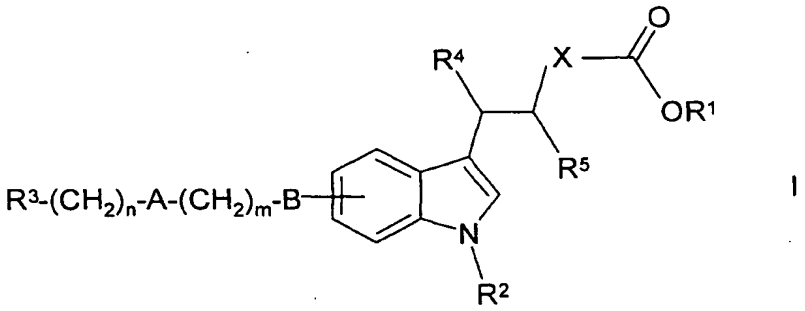
Patent Claims

We Claim:

1. A compound of the formula I



I

in which

A and B are each, independently of one another, O, S, NH, NR^7, CO, CONH, NHCO or a direct bond,

X is alkylene having 1 to 2 carbon atoms which is unsubstituted or monosubstituted by R^4 or R^5, or a direct bond,

R^1 is H, Z or $-(CH_2)_o$-Ar,

R^2 is H, R^7 or -C(O)Z,

R^3 is NHR^6, $-NR^6-C(=NR^6)-NHR^6$, $-C(=NR^6)-NHR^6$, $-NR^6-C(=NR^9)-NHR^6$, Het^1 or $-C(=NR^9)-NHR^6$,

R^4 and R^5 are each, independently of one another, H, oxo, R^7, $-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o-R^7$, $-C(O)-(CH_2)_o$-Het, Het, NHR^6, NHAr, NH-Het, $CONH-R^7$, $CONH-(CH_2)_o$-Ar, $CONH-(CH_2)_o$-Het, OR^7, OAr, OR^6 or O-Het,

R^6 is H, $-C(O)R^7$, -C(O)-Ar, -C(O)-Het, R^7, $COOR^7$, $COO-(CH_2)_o$-Ar, $COO-(CH_2)_o$-Het, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, $-(CH_2)_o$-Ar, $COOR^1$, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, $N(R^1)_2$, $NH-C(O)R^1$, $NHCOOR^1$, COOH, COOZ or $C(O)R^1$,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het is a saturated, partially or fully unsaturated monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members, where 1 or 2 N and/or 1 or 2 S or O atoms may be present and the heterocyclic radical may be monosubstituted or disubstituted by R^8,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

n is 0, 1 or 2,

m is 0, 1, 2, 3, 4, 5 or 6, and

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

2. An enantiomer of a compound according to Claim 1.

3. A compound according to Claim 1, wherein X is a direct bond.

4. A compound according to Claim 1, wherein

B is O,

R^4 is R^7, $(CH_2)_o$-Ar or Het,

o is 0 or 1,

R^5 is H, and

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms.

5. A compound according to Claim 1, selected from,

a) 3-phenyl-3-{6-[3-(pyridin-2-ylamino)propoxy]-1H-indol-3-yl} propionic acid;

b) 3-phenyl-3-[6-(pyridin-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

c) 3-phenyl-3-[6-(benzimidazol-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

d) 3-phenyl-3-[6-(imidazol-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

e) 3-{6-[3-(4,5-dihydro-1H-imidazol-2-ylamino)propoxy]-1H-indol-3-yl}-3-phenylpropionic acid;

f) 3-phenyl -3-[6-[3-(guanidinopropoxy]indol-3-yl}propionic acid;

g) 3-(benzo[1,2,5]thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid;

and physiologically acceptable salts and solvates thereof.

6. A process for the preparation of a compound according to Claim 1 and its salts and solvates, wherein

a) a compound of the formula I is liberated from one of its functional derivatives by treatment with a solvolyzing or hydrogenolyzing agent,

or

b) a radical R^1, R^2, R^3, R^4, R^5 and/or R^6 is converted into another radical R^1, R^2, R^3, R^4, R^5 and/or R^6,

by

i) converting an amino group into a guanidino group by reaction with an amidating agent,

ii) saponifying an ester,

iii) alkylating or acylating an amino group,

iv) converting a cyano group into an amidino group,

and/or a base or acid of the formula I is converted into one of its salts.

7. A therapeutic active ingredient comprising a compound according to Claim 1 and physiologically acceptable salts or solvates thereof.

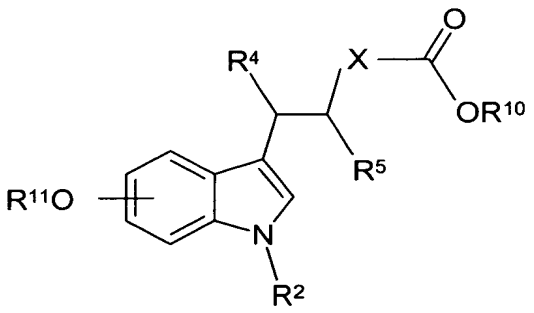
8. An integrin inhibitor comprising a compound according to Claim 1 and physiologically acceptable salts or solvates thereof.

9. A pharmaceutical preparation, comprising at least one compound according to Claim 1 and/or physiologically acceptable salts or solvates thereof.

10. A process for the preparation of a medicament comprising admixing a compound of according to Claim 1 and/or physiologically acceptable salts or solvates thereof with at least one solid, liquid, or semi-liquid excipient or auxiliary or optionally, one or more other active ingredient.

11. A method of treating thromboses, cardiac infarction, coronary heart diseases, arteriosclerosis, inflammations, rheumatic arthritis, macular degenerative disease, diabetic retinopathy, a tumour by inhibition of metastasis, a tumour by initiation of apoptosis, tumour induced angiogenesis disease, osteoporosis, and/or infections and restenosis after angioplasty comprising administering to a patient in need thereof a compound according to Claim 1 and/or physiologically acceptable salts or solvates thereof.

12. Compounds of the formula IIa



IIa

in which R^2, R^4 and R^5 are as defined in Claim 1,

R^1 is H, Z or $-(CH_2)_o$-Ar,

R^2 is H, R^7 or -C(O)Z,

R^4 and R^5 are each, independently of one another, H, oxo, R^7, $-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o-R^7$, $-C(O)-(CH_2)_o$-Het, Het, NHR^6, NHAr, NH-Het, $CONH-R^7$, $CONH-(CH_2)_o$-Ar, $CONH-(CH_2)_o$-Het, OR^7, OAr, OR^6 or O-Het,

R^6 is H, $-C(O)R^7$, -C(O)-Ar, -C(O)-Het, R^7, $COOR^7$, $COO-(CH_2)_o$-Ar, $COO-(CH_2)_o$-Het, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, $-(CH_2)_o$-Ar, $COOR^1$, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, $N(R^1)_2$, $NH-C(O)R^1$, $NHCOOR^1$, COOH, COOZ or $C(O)R^1$,

Het is a saturated, partially or fully unsaturated monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members, where 1 or 2 N and/or 1 or 2 S or O atoms may be present and the heterocyclic radical may be monosubstituted or disubstituted by R^8,

Z is alkyl having 1 to 6 carbon atoms,

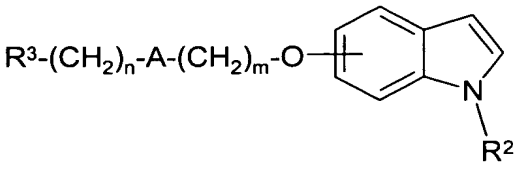
Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

X is a bond, and

R^{10} and R^{11} are each, independently of one another, a hydroxyl-protecting group or H.

13. Compounds of the formula X



X

in which

A is O, S, NH, NR^7, CO, CONH, NHCO or a direct bond,

R^1 is H, Z or $-(CH_2)_o$-Ar,

R^2 is H, R^7 or -C(O)Z,

R^3 is NHR^6, $-NR^6-C(=NR^6)-NHR^6$, $-C(=NR^6)-NHR^6$, $-NR^6-C(=NR^9)-NHR^6$, Het^1or $-C(=NR^9)-NHR^6$,

R^6 is H, -C(O)R^7, -C(O)-Ar, -C(O)-Het, R^7, COOR^7, COO-$(CH_2)_o$-Ar, COO-$(CH_2)_o$-Het, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, -$(CH_2)_o$-Ar, COOR^1, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, N$(R^1)_2$, NH-C(O)R^1, NHCOOR^1, COOH, COOZ or C(O)R^1,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

n is 0, 1 or 2,

m is 0, 1, 2, 3, 4, 5 or 6, and

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

14. A compound according to Claim 1, wherein

X is a bond,

B is O,

R^1 is H,

R^4 is Het,

A is a bond,

and

R^3 is Het^1.

15. A compound according to claim 14, wherein Het^1 is pyridine which may be substituted by NHZ where Z is alkyl having 1 to 6 carbon atoms.

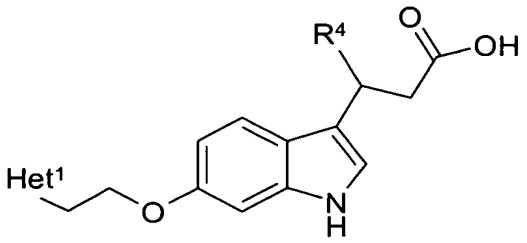
16. A compound according to claim 14, wherein R^4 is benzothiadiazole.

17. A compound according to claim 1, which is 3-(benzo[1,2,5]thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid.

18. A compound according to claim 1, in racemic form.

19. A compound according to claim 1, in the form of substantially only one of its enantiomers.

20. A compound of the formula Ij



Ij

in which

R^3 is NHR^6, $-NR^6-C(=NR^6)-NHR^6$, $-C(=NR^6)-NHR^6$, $-NR^6-C(=NR^9)-NHR^6$, Het^1 or $-C(=NR^9)-NHR^6$,

R^4 is H, oxo, R^7, $-(CH_2)_o-Ar$, $-C(O)-(CH_2)_o-Ar$, $-C(O)-(CH_2)_o-R^7$, $-C(O)-(CH_2)_o-Het$, Het, NHR^6, NHAr, NH-Het, $CONH-R^7$, $CONH-(CH_2)_o-Ar$, $CONH-(CH_2)_o-Het$, OR^7, OAr, OR^6 or O-Het,

R^6 is H, $-C(O)R^7$, -C(O)-Ar, -C(O)-Het, R^7, $COOR^7$, $COO-(CH_2)_o-Ar$, $COO-(CH_2)_o-Het$, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, $-(CH_2)_o-Ar$, $COOR^1$, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, $N(R^1)_2$, $NH-C(O)R^1$, $NHCOOR^1$, COOH, COOZ or $C(O)R^1$,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het is a saturated, partially or fully unsaturated monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members, where 1 or 2 N and/or 1 or 2 S or O atoms may be present and the heterocyclic radical may be monosubstituted or disubstituted by R^8,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

21. A pharmaceutical composition comprising a compound of claim 17 and a pharmaceutically acceptable carrier.

22. A method of treating thromboses, cardiac infarction, coronary heart diseases, arteriosclerosis, inflammations, rheumatic arthritis, macular degenerative disease, diabetic retinopathy, a tumour by inhibition of metastasis, a tumour by initiation of apoptosis, tumour induced angiogenesis disease, osteoporosis, and/or infections and restenosis after angioplasty comprising administering to a patient in need thereof a compound according to Claim 17 and/or physiologically acceptable salts or solvates thereof.